ELECTROCARDIOGRAPHIC PROFILE OF CIRRHOSIS PATIENTS AND ITS RELATION TO CARDIAC DYSAUTONOMIA

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CERTIFICATE

This is to certify that the dissertation titled **"ELECTROCARDIOGRAPHIC PROFILE OF CIRRHOSIS PATIENTS AND ITS RELATION TO CARDIAC DYSAUTONOMIA"** is the bonafide original work of **DR. N.BALAN** in partial fulfillment of the requirements for M.D. Branch – I (General Medicine) Examination of the Tamilnadu DR. M.G.R Medical University to be held in September 2006. The Period of study was from June 2005 to December 2005.

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DECLARATION

I, **DR. N.BALAN,** solemnly declare that the dissertation titled **"ELECTROCARDIOGRAPHIC PROFILE OF CIRRHOSIS PATIENTS AND ITS RELATION TO CARDIAC DYSAUTONOMIA"** is a bonafide work done by me at Govt. Stanley Medical College and Hospital during June 2005 to December 2005 under the guidance and supervision of my unit chief **Prof.A.K.GEETHA DEVI, M.D**., Addl. Professor of Medicine.

This dissertation is submitted to Tamilnadu DR. M.G.R Medical University, towards partial fulfillment of requirement for the award of **M.D. Degree (Branch – I) in General Medicine.**

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CONTENTS

		Page No.
I	INTRODUCTION	1
II	AIM OF THE STUDY	3
III	REVIEW OF LITERATURE	4
IV	MATERIALS AND METHODS	31
V	OBSERVATIONS	35
VI	RESULTS	45
VII	DISCUSSION	48
VIII	CONCLUSION	53
IX	BIBLIOGRAPHY	54

INTRODUCTION

Cirrhosis is a chronic disease of the liver that leads to a number of complications, some of which may eventually prove fatal. There are reports of association of chronic liver disease with autonomic neuropathy.[1]

Patients with chronic liver disease who have associated autonomic neuropathy respond inappropriately or defectively to major events such as septicaemia and variceal haemorrhage.[2] Autonomic Neuropathy (AN) is associated with hemodynamic impairment and with increased vasoactive drug requirements during liver transplantation, probably associated with impaired reflex vasoconstrictor responses to surgical manipulations and changes of blood volume. AN may be associated with a greater surgical risk during liver transplantation. Preoperative evaluation of AN may select a high-risk population of liver transplant recipients.[3]

The present study was undertaken primarily to investigate autonomic functions in hepatic cirrhosis (in both alcoholics and non-alcoholics), analyse characteristics of patients who develop autonomic neuropathy, and to determine the relationship between severity of liver damage and extent of autonomic function impairment.

Electrocardiogram is a very simple and noninvasive investigation in diagnosing asymptomatic autonomic dysfunction. It helps in early recognition of cardiac dysautonomia, which is asymptomatic autonomic dysfunction and precursor of symptomatic autonomic dysfunction. This also helps in taking sufficient precaution to delay or arrest its progression by various measures.

In this study the prevalence of various ECG abnormalities and cardiac dysautonomia in cirrhotic patients are assessed by various ECG markers.

AIMS OF THE STUDY

1) To study the prevalence of various ECG abnormalities in cirrhotic patients as compared to controls.
2) To study the prevalence of cardiac dysautonomia in cirrhotic patients by various ECG markers.

REVIEW OF LITERATURE

HEPATIC CIRRHOSIS

Cirrhosis is a pathologically defined entity that is associated with a spectrum of characteristic clinical manifestations. The cardinal pathologic features reflect irreversible chronic injury of the hepatic parenchyma and include extensive fibrosis in association with the formation of regenerative nodules.[4]

These features result from hepatocyte necrosis, collapse of the supporting reticulin network with subsequent connective tissue deposition, distortion of the vascular bed and nodular regeneration of the remaining liver parenchyma.

The central event leading to hepatic fibrosis is activation of the hepatic stellate cells. Upon activation by factors released by hepatocytes and kupffer cells, the stellate cell assumes a myofibroblast like conformation and under the influence of cytokines such as transforming growth factor β (TGF-β),produces fibril forming type-I collagen. The precise point at which the fibrosis becomes irreversible is unclear.

CAUSES OF CIRRHOSIS[5]

- Alcohol related(most common)
- Chronic vial hepatitis, types B, C, and D
- Primary biliary cirrhosis
- Primary sclerosing cholangitis
- Metabolic diseases
- Autoimmune hepatitis
- Hepatic venous outflow obstruction(Budd Chiari Syndrome, Constrictive Pericarditis)
- Indian childhood cirrhosis
- Toxins and therapeutic agents(Methotrexate, Amiodarone)
- Cryptogenic cirrhosis

CLINICAL FEATURES

Clinical features of cirrhosis derive from the morphologic alterations and often reflect the severity of liver damage than the etiology of the underlying liver disease. Loss of functioning hepatocellular mass may lead to jaundice ,edema, coagulopathy and a variety of metabolic abnormalities ; fibrosis and distorted vasculture lead to portal hypertension and its sequelae, including gastroesophageal varices and splenomegaly. Ascites and hepatic

encephalopathy result from both hepatocellular insufficiency and portal hypertension.[4]

COMPLICATIONS:

The most important complications of cirrhosis are

- Portal hypertension
- Ascites
- Variceal bleeding
- Splenomegaly
- Hepatic encephalopathy
- Hepatorenal Syndrome
- Hepatopulmonary Syndrome
- Hepatocellular carcinoma
- Spontaneous bacterial peritonitis
- Autonomic dysfunction
- Insulin resistance

DIAGNOSIS:

Various investigatory modalities available for the diagnosis of cirrhosis are

- Liver biopsy
- Ultrasound

- CT scan abdomen
- Laparoscopy
- Radioisotope scanning

Since neither liver biopsy nor scanning have a diagnostic sensitivity greater than 90% (USG 87%, biopsy 62%), it has been proposed that ultrasound be done before liver biopsy is performed[6]. If cirrhosis is suspected on ultrasound (or clinical findings) at least two separate liver biopsy specimens should be taken for histology. If histology does not show cirrhosis but the specimen shows fragmentation, fibrosis or architectural disruption, this together with the ultrasound result should allow a diagnosis of cirrhosis to be made.

CHILD-PUGH SCORING.

This is a scoring system developed for staging cirrhotic liver disease. It is used for assessing prognosis and operative mortality of cirrhosis patients. This scoring system is based on both clinical and laboratory parameters namely the levels of bilirubin, albumin, prothrombin time prolongation, the presence of ascites and encephalopathy. Patients are classified as Child class A, B, or C according to the total score of 5–6, 7–9, and 10–15 respectively. The prognosis worsens with increasing score.

CHILD-PUGH SCORING

Parameter	Score		
	1	2	3
Ascites	Absent	Slight to moderate	Tense
Encephalopathy	None	Grade 1–2	Grade 3–4
Albumin(g/l)	>35	28–35	<28
Bilirubin(μmol/l	<34	34–52	>52
Prothrombin time(sec >control)	<4	4–6	>6

CIRRHOSIS AND THE CARDIOVASCULAR SYSTEM:

The cardiovascular effects of cirrhosis are wide-ranging and encompass not only effects on the systemic and splanchnic circulation but also on the heart itself.

Cirrhosis involves the cardiovascular system in the following ways.

1. Cirrhotic cardiomyopathy
2. Autonomic dysfunction
3. Hyperdynamic circulation
4. QT prolongation

Cirrhosis is associated with an increased cardiac output and heart rate as well as decreased systemic peripheral vascular resistance and blood pressure[5].Splanchnic arterial vasodilatation and impaired autonomic activity play a role.[7]

CIRRHOTIC CARDIOMYOPATHY

Cirrhotic cardiomyopathy is recognized with abnormal cardiac contractility particularly with pharmacological and physiological stress[8].A reduction in myocardial β adrenergic receptor signal transduction plays a role, perhaps due to changes in the lipid content of the cardiac plasma membrane or an inhibitory effect of jaundice on adenyl cyclase. Experimental studies have shown decreased β adrenergic receptor density and receptor desensitisation in cardiocytes of cirrhotic rats[9]. In addition, leucocytes of cirrhotic patients also present decreased abundance of β adrenoreceptor[10] .

Heart receptor and post receptor defects are supported by the demonstration of reduced function and expression of cardiac G proteins in cirrhotic animals and impaired cardiac excitation-contraction coupling in portal hypertensive rats[11] .Plasma membrane fluidity and ion channel function are impaired in cirrhosis.[12]

Left ventricular wall thickness may be increased. The cause of increased cardiac wall thickness is not fully understood. But the role of renin angiotensin aldosterone system (RAAS) and adrenergic hyperactivity has been considered. While systolic function is well preserved at rest there is chronotropic and inotropic incompetence on exercise[13].

Left ventricular ejection fraction is decreased on exercise. The failure of the ejection fraction to increase despite an increase in venous return is suggestive of diastolic dysfunction[13].

Cardiac dysfunction may be subclinical, presenting only after liver transplantation[5]. This may presumably due to the reduction in after-load that accompanies the generalized vasodilatation of advanced liver disease[13].

Studies using brain natriuretic peptide (BNP) as a marker of high ventricular pressure reflecting Cardiac dysfunction have shown that the levels of BNP correlated closely with the severity of Cirrhosis as measured by Child-Pugh class and also the degree of Portal hypertension as measured by hepatic venous pressure gradient[13].Changes were seen equally in patients with alcoholic and nonalcoholic liver diseases.

PATHOGENESIS OF AUTONOMIC DYSFUNCTION AND HYPERDYNAMIC CIRCULATION:

Hyperdynamic circulation is a common and long-recognized feature of patients with advanced cirrhosis[14], consisting of elevated cardiac rate and output and reduced peripheral vascular resistance, so that arterial pressure is tendentially or frankly reduced[14]. Owing to the importance of autonomic function in cardiovascular homeostasis, it may be involved in the pathogenesis of the hyperdynamic circulation.

The setting of the hyperdynamic circulatory syndrome is the pathogenetic background of complications such as renal sodium and water retention and hepatorenal syndrome[15].

CAUSES FOR HYPERDYNAMIC CIRCULATION[16,17]

1. Splanchnic blood pooling
2. Opening of portal-systemic collaterals
3. Arterial vasodilation, mainly splanchnic
4. Compensatory increase in blood volume

The pathogenesis of arterial vasodilation is still debated. It has been well recognized that blood nor-adrenaline levels are elevated in cirrhotic patients[18,19]

Baseline nor-adrenaline levels correlate positively with the severity of the cirrhosis[20]. There has been no satisfactory explanation for this observation[18]. The high Nor- Epinephrine (NE) levels can be reduced by head-out water immersion testing, suggesting that a decreased effective plasma volume may be the stimulus for the increased secretion of endogenous NE[21].

It is known that nor-epinephrine levels are affected by a variety of factors, including metabolism in the liver and neuronal uptake and intraneuronal metabolism. There is no current evidence to suggest that a defect in the metabolism of nor-epinephrine in the liver contributes significantly to excessive plasma nor-epinephrine[22]..Neuronal up-take and intraneuronal metabolism of nor-epinephrine, however, have not been studied in cirrhotics. It is possible that the excessive nor-epinephrine is a compensatory response to vasodilatation and other hemodynamic changes seen in liver disease. In addition, there may be alterations of end-organ responsiveness, leading to a reduction in the pressor effects of NE.

It has been suggested that the decreased vascular sensitivity of patients with ESLD to vasoconstrictors in the presence of increased levels of

vasodilators (glucagon, atrial natriuretic factor, platelet-activating factor, bile salts) is responsible for this hyper dynamic circulatory state. Metabolites of nitric oxide (nitrites and nitrates) are also increased in ESLD. Moderately increased levels of endothelin-1 in patients with ESLD can also contribute to vasodilatation by stimulating synthesis of nitric oxide in the endothelium.

It has been hypothesised that a porto-systemic shunt may diminish the hepatic clearance of gut derived vasoactive agents.

Blood volume expansion follows renal retention of sodium and water, which, in turn, is evoked by secondary hyperaldosteronism, activation of sympathetic nervous system, enhanced secretion of arginine vasopressin,and reduced renal perfusion[23,24].

AUTONOMIC DYSFUNCTION (AD)

Autonomic Dysfunction can contribute to the hyper dynamic circulatory syndrome in several ways. A sympatho-vagal imbalance with a prevalent parasympathetic dysfunction would lead to a defective inhibitory vagal tone on the cardiac pacemaker. An acceleration of heart rate would ensue and contribute to increased cardiac output along with an enhanced cardiac preload[25]. Moreover, in the subset of patients with defective sympathetic

function, this may contribute to the blunted cardiovascular response to adrenergic vasoconstrictors and maneuvers enhancing the sympathoadrenergic drive, which have been described in cirrhosis[26,27]

AD is commonly detected in patients with cirrhosis, and its prevalence increases in parallel with the severity of liver disease, as does the hyper dynamic circulatory syndrome. Moreover, the presence of both abnormalities heralds an adverse prognosis[28,26].

Desperate events may contribute to the development of AD, including factors affecting nerve integrity, such as alterations in lipid metabolism, vitamin E deficiency, alcohol intake, immunologic mechanisms, and retention of toxic metabolites[29].Moreover, vagal function may be inhibited by elevated angiotensin II production[30]

This abnormality of the nervous system appears to be unrelated to the toxic effects of chronic alcohol use, because cross-sectional studies have shown an equal prevalence of AN in alcohol and non–alcohol related liver disease. The autonomic neuropathy is probably related to the changes resulting from liver disease, although the precise mechanism remains unclear.

Cold pressor tests suggest that cirrhotic patients have relative hyporesponsiveness to ά-adrenoreceptor stimulation. The failure of these compensatory mechanisms in the presence of overwhelming stress may explain the apparent increase in mortality in patients with chronic liver disease and autonomic neuropathy.

QTc PROLONGATION

AD is associated with an impairment of free water generation and hyponatremia [31,32], and is likely involved in the pathogenesis of prolonged electrocardiographic Q-T interval [33], a common finding in advanced cirrhosis with an adverse prognostic significance [34]. The QT interval on ECG is frequently prolonged. Correction of the prolonged QT interval has been documented in post transplant patients.

Recently, Ward and colleagues [35] described a decrease in K+ current in ventricular myocytes of cirrhotic rats, which would result in a tendency to prolong QT intervals. This is in agreement with the results of Bernardi and colleagues showing a prolonged QT interval and other electrophysiological abnormalities in cardiac excitation and repolarisation in cirrhotic patients. It has been suggested that androgen deficiency may also cause Q-Tc prolongation in male patients with cirrhosis.[36]

CLINICAL FEATURES OF AUTONOMIC NEUROPATHY[37]

SYSTEM	SYMPTOMS
1. Cardiovascular	1. Postural hypotension
	2. Painless MI
	3. Resting tachycardia
	4. Loss of heart rate variation
2. Gastrointestinal	1. Esophageal dysmotility
	2. Gastric atony
	3. Diarrhoea
	4. Colonic atony
3. Respiratory	1. Respiratory arrest
4. Urogenital	1. Bladder dysfunction
	2. Impotence
	3. Retrograde ejaculation
	4. Loss of testicular sensation

5. Pupillary abnormalities	1. Reduced resting diameter 2. Delayed (or) absent response to light. 3. Diminished hippus
6. Vasomotor	1. Loss of skin Vasomotor Responses 2. Peripheral vascular changes 3. Dependent edema
7. Sudomotor	1. Anhydrosis 2. Gustatory sweating

AUTONOMIC NERVOUS SYSTEM

The nervous system is divided into the somatic nervous system which controls organs under voluntary control (mainly muscles) and the Autonomic Nervous System (ANS) which regulates individual organ function and

homeostasis, and for the most part is not subject to voluntary control. It is also known as the visceral or automatic system.

The ANS is predominantly an efferent system transmitting impulses from the Central Nervous System (CNS) to peripheral organ systems. Its effects include control of heart rate and force of contraction, constriction and dilatation of blood vessels, contraction and relaxation of smooth muscle in various organs, visual accommodation, pupillary size and secretions from exocrine and endocrine glands.

Autonomic nerves constitute all of the efferent fibres which leave the CNS, except for those which innervate skeletal muscle. There are some afferent autonomic fibres (i.e. transmit information from the periphery to the CNS) which are concerned with the mediation of visceral sensation and the regulation of vasomotor and respiratory reflexes, for example the baroreceptors and chemoreceptors in the carotid sinus and aortic arch which are important in the control of heart rate, blood pressure and respiratory activity. These afferent fibres are usually carried to the CNS by major autonomic nerves such as the vagus, splanchnic or pelvic nerves, although afferent pain fibres from blood vessels may be carried by somatic nerves.

The ANS is primarily involved in reflex arcs, involving an autonomic or somatic afferent limb, and then autonomic and somatic efferent limbs. For instance, afferent fibres may convey stimuli from pain receptors, or mechanoreceptors and chemoreceptors in the heart, lungs, gastrointestinal tract etc.

There may then be a reflex response to this involving autonomic efferent fibres causing contraction of smooth muscle in certain organs (e.g. blood vessels, eyes, lungs, bladder, gastrointestinal tract) and influencing the function of the heart and glands. The efferent limbs of these reflexes may also involve the somatic nervous system (e.g. coughing and vomiting). Simple reflexes are completed entirely within the organ concerned, whereas more complex reflexes are controlled by the higher autonomic centres in the CNS, principally the hypothalamus.

The ANS is divided into two separate divisions called the Parasympathetic and Sympathetic Systems, on the basis of anatomical and functional differences. Both of these systems consist of myelinated preganglionic fibres which make synaptic connections with unmyelinated postganglionic fibres, and it is these which then innervate the effector organ. These synapses usually occur in clusters called ganglia. Most organs are innervated by fibres from both divisions of the ANS, and the influence is

usually opposing (e.g. the vagus slows the heart, whilst the sympathetic nerves increase its rate and contractility), although it may be parallel (e.g. the salivary glands). Parasympathetic fibres from the vagus (through acetyl choline) and sympathetic fibres (through nor-adrenaline) from upper 4 to 5 thoracic ganglion innervate heart and mediate autonomic control.

CARDIAC DYSAUTONOMIA [38]

Cardiac dysautonomia refers to autonomic dysfunction of heart. It appears to be the most frequent autonomic dysfunction in patients with cirrhosis. There are two terms.

1. Autonomic Neuropathy

Refers to combined and objective evidence of autonomic involvement.

2. Autonomic Dysfunction

Refers to abnormal cardiovascular tests in absence of clinical symptoms.

Autonomic Dysfunction in cirrhosis with portal hypertension is common but symptomatic autonomic neuropathy is less common.

EFECTS OF SYMPATHOVAGAL IMBALANCE [39]

1. Impairs angina recognition.
2. Alters threshold for ischemia
    -increased heart rate and blunted chronotropic response to exercise.
    -impaired coronary casomotor regulation.
3. Abnormailty in diastolic and systolic function.
    -contributes to cardiomyopathy.
4. Increased risk of ventricular arrhythmia
    - contributes to sudden cardiac death.
5. Altered circadian pattern of triggering acute cardiac events
    -leads to loss of nocturnal protection against acute MI.
6. Altered circadian blood pressure regulation leads to
    - increased cardiac mass
    -causes haemodynamic instability in perioperative period.

CLINICAL PRESENTATION

Autonomic damage may be asymptomatic and thus be detected incidentally, even if symptomatic, the condition goes unnoticed for a considerable period of time partly because of the vagueness of many of early

symptoms. The proportion of asymptomatic subjects increases with increasing duration of the disease.

The features of cardiac autonomic neuropathy include

1. Exercise intolerance
2. Postural hypotension
3. Resting tachycardia
4. Fixed heart rate.
5. Silent myocardial infarction.

Chronic liver disease has been shown to be associated with autonomic neuropathy (AN) as well as hemodynamic and circulatory disturbances. [1]

This abnormality of the nervous system appears to be unrelated to the toxic effects of chronic alcohol use, because cross-sectional studies have shown an equal prevalence of AN in alcohol- and non–alcohol-related liver disease.

In a longitudinal study in patients with Child A liver disease, the 4-year mortality was found to be 30% in patients with autonomic neuropathy compared with 6% in patients without autonomic dysfunction multiple logistic

regression analysis showed that the presence of autonomic neuropathy and severity of liver disease were independent risk factors of mortality[40].

EXERCISE INTOLERANCE

Patients with Autonomic Neuropathy achieve a lower heart rate, blood pressure and cardiac output on exercise compared to normal people.

POSTURAL HYPOTENSION

Dizziness, fainting blackouts or visual impairment on standing are the clinical presentations of Postural hypotension and it is the most prominent and disabling cardiovascular manifestation of Autonomic Neuropathy. The blood pressure fall may be worsened by a variety of drugs like diuretics and hypotensive agents including β blockers and nitrates.

The main lesion in Postural hypotension is probably in the efferent limb of the reflex with damaged sympathetic vasoconstrictor fibres in the splanchnic bed, muscle and skin. The hypotension may be augmented by a diminished plasma rennin response on standing, which is due to impaired sympathetic innervation to juxtaglomerular apparatus, one of the sequelae of autonomic dysfunction.

RESTING TACHYCARDIA

The mean resting heart rate of patients with cirrhosis of the liver has been found to be increased when compared to the controls due to the presence of autonomic neuropathy in these patients.

Vagal tone, as assessed by baroreflex sensitivity is markedly depressed in cirrhotic patients awaiting liver transplantation[41]. This is the reason for resting tachycardia in many cirrhotics.

FIXED HEART RATE

Chronic liver disease is accompanied by a significant Heart Rate Variability decrease. Heart rate shows less diurnal variation with increasing autonomic damage. Loss of the normal cardiac slowing at night results from vagal damage. With severe damage there is a loss of minute to minute and second to second variation in heart rate, resulting in relatively fixed heart rate.

SILENT MYOCARDIAL INFARCTION

Autonomic Neuropathy may reduce the perception of cardiac ischaemic pain. The incidence of coronary artery disease is low in cirrhotics. It is only about a quarter of that among total cases examined without cirrhosis. Cirrhotics

are less liable to coronary and aortic atheroma than the rest of the population[5]. This may also be due to the low peripheral vascular resistance in these patients.

ECG CHANGES IN CIRRHOTICS

The QT interval is an approximate measure of ventricular electrical recovery after excitation. A prolonged QT interval identifies patients at increased risk for sudden cardiac death in a variety of clinical situations, in patients with alcohol-related liver disease (ALD) who continue to drink to excess, QT prolongation is associated with sudden death due to arrhythmias[42] . The cause of QT prolongation in liver disease is not clear.

A relationship between the severity of autonomic damage and extent of the QT corrected for heart rate (QTc) prolongation in ALD and non-ALD has been reported, and it was suggested that autonomic neuropathy was the cause of the prolonged QT interval. Liver transplantation reverses prolonged QT interval. The etiology of liver disease did not affect the prevalence of abnormal QTcmax interval. Prolonged QT interval correlated positively with increasing severity of liver disease, as indicated by the Child-Pugh score.

Another important ECG change noted commonly in cirrhotics is the decreased variation of electrocardiographic R-R interval.

ASSESSMENT OF CARDIOVASCULAR AUTONOMIC DYSFUNCTION

Objective measurement of autonomic nerve damage is based on cardiovascular reflexes as these are reliable and quantitative noninvasive methods to access autonomic nervous system function. Implicit in the use of cardiovascular reflex test is the assumption that it reflects damage throughout the autonomic nervous system. This is largely true except for the very early manifestation such as sweating loss on the feet and impotence which may antedate abnormal cardiovascular tests.

TESTS FOR PARASYMPATHETIC FUNCTION

1. Heart rate response to deep breathing
2. Heart rate response to standing
3. Heart rate response to valsalva maneuver

TESTS FOR SYMPATHETIC FUNCTION

1. BP response to standing
2. BP response to sustained hand grip.

CARDIAC AUTONOMIC FUNCTION TESTS

CARDIAC AUTONOMIC FUNCTION TESTS	NORMAL	ABNORMAL
heart rate response to deep breathing(E:I ratio)	≥ 1.1	< 1.1
heart rate response to standing (30:15 ratio)	> 1.04	< 1.0
Valsalva ratio	> 1.21	< 1.20
BP response to standing (fall in systolic BP)	<10mmHg	> 20 mm Hg
BP response to sustained hand grip (increase in diastolic BP)	>16mmHg	<10mmHg

HEART RATE VARIATION ON DEEP BREATHING

The normal acceleration and deceleration of heart rate during respiration (sinus arrhythmia) is reduced early in course due to cardiac vagal involvement.

This phenomenon provides the basis for the simplest and most sensitive test for the presence of cardiac dysautonomia.

The patient takes breath deeply and evenly at a rate of six breaths per minute, i.e. five seconds for inspiration and five seconds for expiration. The ratio of the mean of the longest RR interval during expiration to the mean of the shortest RR interval during inspiration is calculated from the ECG recording. This is called the E: I ratio and it indicates autonomic dysfunction if < 1.1.

HEART RATE RESPONSE TO VALSALVA MANOEUVRE

The subject was seated quietly and then asked to blow into a mouthpiece attached to a manometer, holding it at a pressure of 40 mm Hg for 15 seconds while a continuous electrocardiogram (ECG) was recorded. The manoeuvre was repeated three times with one minute interval in between and results were expressed as:

$$\text{Valsalva ratio} = \frac{\text{longest R-R interval after the manoeuvre}}{\text{Shortest R-R Interval during the manoeuvre}}$$

The mean of the three Valsalva ratios was taken as the final value.

IMMEDIATE HEART RATE RESPONSE TO STANDING

The test was performed with the subject lying quietly on a couch while the heart rate was recorded continuously on an electrocardiograph. The patient was then asked to stand unaided and the point at starting to stand was marked on ECG paper. The shortest R-R interval at or around the 15th beat and the longest R-R interval at around the 30th beat after starting to stand were measured with a ruler. The characteristic heart rate response was expressed by 30:15 ratios.

BLOOD PRESSURE RESPONSE TO STANDING

This test measured the subject's blood pressure with a sphygmomanometer while he was lying quietly and one minute after he was made to stand up. The postural fall in blood pressure was taken as the difference between the systolic pressure lying and the systolic blood pressure standing. The test was repeated three times and the mean was calculated.

BLOOD PRESSURE RESPONSE TO SUSTAINED HAND GRIP

The blood pressure of the patient was taken three times before the manoeuvre. A sphygmomanometer was used for sustained handgrip manoeuvre. The patient was asked to grip the inflatable rubber bag and apply maximum voluntary pressure possible. The reading during maximum voluntary

contraction is noted. Thereafter, the patient was asked to maintain 30% of maximum voluntary contraction for as long as possible up to five minutes. Blood pressure was measured at one minute intervals during the handgrip. The result was expressed as the difference between the highest diastolic blood pressure during the handgrip exercise and the mean of the three diastolic blood pressure readings before the handgrip began.

MATERIALS AND METHODS

STUDY POPULATION

Study group- 50 patients with cirrhosis with portal hypertension

Control group- 50 age and sex matched controls.

PLACE OF STUDY

Department of Medicine

Department of Gastroenterology

Stanley Medical College

Chennai-1

PERIOD OF STUDY

June 2005 to December 2005

METHODS

All the study group patients and controls were subjected for thorough physical examination. Blood samples were drawn and subjected to estimation of estimation of liver function, renal function and glucose levels.

EXCLUSION CRITERIA

1. Age above 60 years.
2. Documented ischemic heart disease
3. Documented valvular/congenital heart disease
4. Hypertension and Diabetes mellitus.
5. Chronic obstructive pulmonary disease
6. Drugs-β blockers, digoxin, calcium channel blockers
7. Features of hypothyroidism
8. Uraemia
9. Features of parkinsonism and rheumatoid arthritis

Cardiovascular autonomic dysfunction was assessed by the following maneuvers.

PARASYMPATHETIC FUNCTION

1. Tachycardia in resting ECG
2. heart rate response to deep breathing(E:I ratio)

SYMPATHETIC FUNCTION

1. BP response to standing
2. QTc prolongation

ELECTROCARDIOGRAM

Resting ECG was taken in both the study and control group using a three leaded Schiller Cardiovit AT machine. ECG during deep breathing was recorded only in the study group using single leaded BPL ECG machine. The lead considered here is lead II.

The subjects were made to lie down quietly. Then they were asked to take deep breath in and out at a rate of six breaths per minute (i.e) five seconds for inspiration and five seconds for expiration which produces a maximum heart rate variation. A continuous ECG was recorded for one minute.

E: I ratio was measured which is the ratio of the mean of the longest RR interval during expiration to the mean of the shortest RR interval during inspiration. it indicates autonomic dysfunction if < 1.1.

QTc INTERVAL

R-R and QT intervals are measured with a meter on the resting ECG tracing. The lead considered here is lead V_2.The QT interval was measured from the beginning of the QRS complex to the end of the downslope of the T

wave (crossing the isoelectric line). When a 'U' wave was present, the QT interval was measured to the nadir of T and U waves.

The corrected QT interval for the previous cardiac cycle length (QTc) was calculated using Bazett's formula[43]

$$QTc = \frac{QT}{\sqrt{R\text{-}R(sec)}}$$

A QTc >460 msec is considered abnormally prolonged.

BLOOD PRESSURE RESPONSE TO STANDING

This test measured the subject's blood pressure with a sphygmomanometer while he was lying quietly and one minute after he was made to stand up. The postural fall in blood pressure was taken as the difference between the systolic pressure lying and the systolic blood pressure standing. The test was repeated three times and the mean was calculated. The test is taken as positive when the fall in systolic blood pressure was more than 20 mm Hg.

OBSERVATIONS

AGE DISTRIBUTION

AGE IN YEARS	CONTROL GROUP		STUDY GROUP	
	NO.	%	NO	%
10-20	6	12	6	12
21-30	3	6	2	4
31-40	12	24	15	30
41-50	22	44	20	40
51-60	7	14	7	14

More than half of the study populations were above 40 years of age.

Most number of patients (40%) belonged to the age group of 41-50 years.

STUDY GROUP (CIRRHOTICS) & DISEASE DURATION

DURATION	NO. OF PATIENTS	PERCENTAGE
0-1 yr	28	56
1-2 yrs	9	18
2-3 YRS	4	8
3-4 yrs	6	12
>4 yrs	3	6

56% of the Cirrhotics have duration of the disease less than a year.

STUDY GROUP (CIRRHOTICS) & CHILD'S GRADING

CHILD-PUGH CLASS	NO.OF PATIENTS	PERCENTAGE
A	4	8
B	42	84
C	4	8
TOTAL	50	100

Maximum number of patients belonged to class B (84%)

ECG ABNORMALITIES

RESTING HEART RATE

GROUPS	RESTING HEART RATE	
	Range (bpm)	Mean (bpm)
Study (Cirrhotics)	63-133	90 ± 16.98
Control	56-108	76.78 ± 11.23

*p = 0.0006 *Unpaired't' test

The mean resting heart rate of the Study group (Cirrhotics) (90 ± 16.98 bpm) is significantly higher ($p<0.05$) than that of Control group (76.78 ± 11.23 bpm).

R-R INTERVAL

GROUPS	R-R INTERVAL	
	Range (msec)	**Mean (msec)**
Study (Cirrhotics)	451 – 952	690.54 ± 133.38
Control	562 – 1071	797.98 ± 119.17

*t = 4.24 p = 0.001 *Unpaired‘t’ test

R-R Interval of Study group (690.54 ± 133.38 msec) is significantly lower than Control group (797.98 ± 119.17 msec) ($p<0.005$) correlating with increased resting heart rate signifying parasympathetic damage.

P-R INTERVAL

GROUPS	P-R INTERVAL	
	Range (msec)	**Mean (msec)**
Study (Cirrhotics)	96 – 176	139.36 ± 19.09
Control	118 – 200	143.76 ± 18.62

*t = 1.17 p=0.24 *Unpaired‘t’ test

Both Study and Control Group show no statistically significant difference in P-R Interval ($p<0.05$).

QRS DURATION

GROUPS	QRS DURATION	
	Range (msec)	**Mean (msec)**
Study (Cirrhotic)	60 – 120	58 ± 15.28
Control	40– 80	58.4 ± 12.18

*p=0.2675

*Mann-Whitney Test

Both Study and Control Group show no statistically significant difference in QRS Duration (p>0.05).

QRS AXIS

GROUPS	QRS AXIS	
	Range (degrees)	**Mean (degrees)**
Study (Cirrhotics)	-36 - +120	42.12 ± 31.64
Control	0 - +100	48.92 ± 23.38

*t = 1.22 p=0.22

*Unpaired‘t’ test

Both Study and Control Group show no statistically significant difference in QRS Axis (p>0.05).

QTc INTERVAL

GROUPS	QTc INTERVAL	
	Range (msec)	**Mean (msec)**
Study (Cirrhotic)	350 – 501	430.14 ± 41.43
Control	312 – 498	376.36 ± 36.54

*t = 6.88 p = 0.001

*Unpaired‘t’ test

QTc Interval of Study group (430.14 +/- 41.43 msec) is significantly prolonged than Control group (376.36 +/- 36.54 msec) ($p<0.005$).

E: I RATIO

STUDY GROUP (CIRRHOTICS)

E:I RATIO	NO. OF PATIENTS	PERCENTAGE
Normal (≥ 1.1)	27	54
Abnormal (< 1.1)	23	46

46% of Study Group has abnormal E: I Ratio, which is suggestive of an early parasympathetic dysfunction.

SIGNIFICANT POSTURAL DROP OF SYSTOLIC BP (>20 mmHg)

POSTURAL DROP OF SBP(>20 mmHg)	NO. OF PATIENTS	PERCENTAGE
Study (Cirrhotics)	6	12
Control	0	0

12% of the Study Group show significant Postural Drop of SBP (>20 mmHg) on standing which probably indicates sympathetic nervous system dysfunction.

COMPARISON OF QTc PROLONGATION IN PATIENTS & CONTROLS

GROUPS	QTc PROLONGATION	PERCENTAGE
Study (Cirrhotics)	10	20
Control	2	4

This study shows that QTc prolongation is common (20%) in patients when compared to Control Group (4%).

CHILD – PUGH GRADING & QTc PROLONGATION

Child Grading	No of Patients	QTc Prolongation	%
A	4	0	0
B	42	8	19
C	4	2	50
Total	50	10	20

There is a positive correlation between QTc Prolongation and increasing severity of Cirrhosis.

CHILD – PUGH GRADING & CARDIAC DYSAUTONOMIA

CHILD GRADING	NO OF PATIENTS	E: I RATIO <1.1	PERCENTAGE
A	4	0	0
B	42	19	45
C	4	4	100
Total	50	23	46

There is a positive correlation between Disease Severity and Parasympathetic Dysfunction.

CORRELATION BETWEEN DISEASE SEVERITY & POSTURAL DROP OF SBP >20MMHG

CHILD GRADING	NO OF PATIENTS	POSTURAL DROP OF SBP >20MMHG	PERCENTAGE
A	4	0	0
B	42	4	9.5
C	4	2	50
Total	50	6	12

There is a positive correlation between Disease Severity and Sympathetic Dysfunction.

This Study shows that all the patients with Sympathetic Dysfunction had Parasympathetic Dysfunction as well.

CORRELATION BETWEEN ALCOHOLISM & QTc PROLONGATION

GROUPS	NO. OF PATIENTS	MEAN QTc INTERVAL
Alcoholics	23	426.30 ± 37.11
Non-Alcoholics	27	433.40 ± 45.22

*t = 0.6 p = 0.55 *Unpaired‘t’ test

Both the Groups show that there is no statistically significant difference in QTc Interval.

CORRELATION BETWEEN GI BLEED & QTc INTERVAL

GROUPS	NO OF PATIENTS	MEAN QTC INTERVAL
Bleeders	34	428.176 ± 41.82
Non-Bleeders	16	434.31 ± 41.62

*t = 0.48 p = 0.63 *Unpaired‘t’ test

There is no statistically significant difference in QTc Interval between Bleeders & Non-Bleeders.

CORRELATION BETWEEN SEX OF THE PATIENT & QTc INTERVAL

GROUPS	NO OF PATIENTS	MEAN QTc INTERVAL
Male	39	435.61 ± 39.026
Female	11	410.72 ± 45.734

*t = 1.8 p = 0.08 *Unpaired‘t’ test

There is no statistically significant difference in QTc Interval between Male and Female Patients.

CORRELATION OF CARDIAC DYSAUTONOMIA BETWEEN BLEEDERS & NON-BLEEDERS

GROUP	NO OF PATIENTS	PARASYMPATHETIC DYSFUNCTION		BOTH(PARASYM & SYMP DYSFN)	
		No of Pts	%	No of Pts	%
Bleeders	34	21	61.7	5	14.7
Non-bleeders	16	2	12.5	1	6.2

This study shows Cardiac dysautonomia is commoner in Bleeders when compared to Non-Bleeders.

RESULTS

1) The Resting Heart rate in Cirrhotics (90 ± 16.98 bpm) was significantly ($p<0.05$) higher than that of Controls (76.78 ± 11.23 bpm).

2)The R-R Interval of Study group (690.54 ± 133.38 msec) is significantly lower than Control group (797.98 ± 119.17 msec) ($p<0.005$) correlating with increased resting heart rate signifying parasympathetic damage.

3) Both Study (139.36 ± 19.09 msec) and Control Group (143.76 ± 18.62 msec) show no statistically significant difference in P-R Interval ($p>0.05$).

4) The QRS Duration in Study Group(77.68 ± 10.87 msec) and Control Group(65.28 ± 12.77 msec) showed no statistically significant difference ($p>0.05$).

5) The QRS Axis in Study Group (42.12 ± 31.64 degrees) and Control Group (48.92 ± 23.38 degrees) show no statistically significant difference ($p>0.05$).

6) The QTC Interval of Study group (430.14 +/- 41.43 msec) is significantly prolonged than Control group (376.36 +/- 36.54 msec) ($p<0.005$).

7) 46% of Study Group have abnormal E:I ratio which is suggestive of an early parasympathetic dysfunction.

8) 12% of the Study Group show significant Postural Drop of SBP (>20 mmHg) on standing which probably indicates sympathetic nervous system dysfunction.

9) This study shows that QTc prolongation is common (20%) in patients when compared to Control Group (4%).

10) QTc prolongation was seen in none of the patients in Child ‘A’ , 19% in Child ‘B’ and 50% in Child ‘C’. So there is a positive correlation between QTc Prolongation and increasing severity of Cirrhosis.

11) Parasympathetic Dysfunction (E: I Ratio <1.1) was seen in none of the patients in Child ‘A’ , 45% in Child ‘B’ and 100% in Child ‘C’. So there is a positive correlation between Disease Severity & Parasympathetic Dysfunction.

12) Sympathetic Dysfunction (Postural Drop of SBP >20mmHg) was seen in none of the patients in Child ‘A’ , 9.5% in Child ‘B’ & 50% in Child ‘C’. There is a positive correlation between Disease Severity & Sympathetic Dysfunction.

13) None of the patients had Sympathetic Dysfunction alone. All the patients with Sympathetic Dysfunction had Parasympathetic Dysfunction as well.

14) There is no statistically significant difference in QTc Interval ($p>0.05$) between Alcoholics (426.30 ±37.11 msec) & Non-Alcoholics (433.4 ±45.22 msec).

15) There is no statistically significant difference in QTc Interval ($p>0.05$) between Bleeders (428.176 ± 41.82 msec) & Non-Bleeders (434.31 ± 41.62 msec).

16) There is no statistically significant difference in QTc Interval ($p>0.05$) between male (435.61 ± 39.026 msec) and female patients (416.72 ± 45.734msec).

17) Parasympathetic Dysfunction is seen in 61.7% of Bleeders & 12.5% of Non-Bleeders while both Parasympathetic & Sympathetic Dysfunction is seen in 14.7% of Bleeders & 6.2% of Non-Bleeders. So this study shows that Cardiac dysautonomia is commoner in Bleeders when compared to Non-Bleeders.

DISCUSSION

This study compares the ECG Changes of 50 Cirrhotic Patients with equal numbers of Age & Sex matched Control populations. By using various ECG Parameters, this study also delineates the prevalence of Autonomic Dysfunction in Cirrhosis with Portal Hypertension Patients.

The Mean Resting Heart Rate is found to be 90 bpm in the Study Group as compared to 76.78 bpm in the Control Group. Thus the Resting Heart Rate is nearly 12 bpm more in the Study Group than that of Control Group.

This is probably due to Cardiac Autonomic Dysfunction, more specifically parasympathetic damage. Ewing et al[44]have found that the parasympathetic nerves are the earliest to be involved followed by sympathetic nerves in autonomic neuropathy.

The Study (139.36 ± 19.09 msec) and Control Group (143.76 ± 18.62 msec) showed no statistically significant difference in P-R Interval and QRS duration in the study.

The QRS Axis in Study Group (42.12 ± 31.64 degrees) and Control Group (48.92 ± 23.38 degrees) showed no statistically significant difference ($p>0.05$).

The QTC Interval of Study group (430.14 +/- 41.43 msec) is significantly prolonged than that of Control group (376.36 +/- 36.54 msec) ($p<0.005$).

This study showed that QTc prolongation (20% of patients) is a frequent finding in patients with liver disease. The prolongation of QTc interval correlated with the severity of liver damage and occurred independent of etiology. This data also confirm previous observations that autonomic dysfunction is common in patients with chronic liver disease irrespective of etiology. [1, 45]

Govin et al[46] stated that QTc prolongation can be taken as a marker of autonomic neuropathy, especially cardiac sympathetic innervation damage.

IMPLICATIONS OF PROLONGED QTc INTERVAL

1) For identifying patients who are prone to syncopal attack due to ventricular arrhythmia.

2) Among patients with previous MI a prolonged QTc interval doubles the risk of sudden death.
3) QT prolongation is one of the primary electrical syndromes responsible for sudden cardiac death, so measurement of the same in the ECG of Cirrhotics is of paramount importance of assessing the risk of sudden cardiac death.

In my Study, Parasympathetic Dysfunction is seen in 46% of patients whereas Sympathetic Dysfunction is seen in 12% of patients. All patients with Sympathetic Dysfunction also showed evidence of Parasympathetic Dysfunction.

In a study done by Bajaj et al, 16 of the 20 cirrhotics (80%) were found to have an abnormal result in one or more autonomic function tests[47]. However, Barter and Tanner in their study of 30 subjects reported evidence of parasympathetic damage in 16% and of combined parasympathetic and sympathetic neuropathy in an additional 20%[48]. The lower frequency of autonomic dysfunction in their study could be due to the fact that they included only 14 subjects with alcoholic liver disease while the rest had an alcohol dependence problem only. Szalay *et al* in their evaluation of 121 patients with chronic alcoholism—33 without liver disease, 33 with fatty liver, 33 with cirrhosis, 10 with biliary cirrhosis, and 12 with cirrhosis of another origin—

found autonomic reflex damage in all.[49] They observed significantly more damage in those with liver disease.

Hendrickse and Triger reported cardiovascular autonomic dysfunction with predominantly parasympathetic abnormality in 35% of the patients with chronic liver disease.[50]Hendrickse *et al* in another study reported vagal neuropathy in 45% of the 60 patients of chronic liver disease studied.[43] The vagal function was more commonly affected than the sympathetic function.

Although this disparity may reflect an earlier impairment of the vagal branch owing to possibly greater vulnerability of parasympathetic fibers,[51] the fact that tests based on heart rate changes are much more sensitive than those based on blood pressure variations in revealing subtle autonomic defects cannot be overlooked.[52] In fact, when the sympathetic pathway was evaluated with the sweat test, which has a higher sensitivity, the prevalence of its alteration approached that of vagal dysfunction.[53] Similar findings were also observed by evaluating beat-to-beat fluctuation in heart rate by power spectral analysis.[54] Gentile et al found autonomic neuropathy in 60% (71% in the alcoholic group and 57% in the non-alcoholic group) of the 113 cirrhotics studied.[55] Like in the present study, alteration of parasympathetic function was significantly more frequent than that of sympathetic function. Dillon *et al* also detected abnormal cardiovascular reflexes in 60% of 70 cirrhotics[56].

In the present study, 19 (45%) out of 42 patients belonging to Child class B had autonomic dysfunction while all the four (100%) patients in class C had impaired autonomic function. These findings are similar to the observations of most other studies, which reported increasing frequency of autonomic dysfunction with increasing severity of liver damage. Hendrickse and Triger reported a strong correlation between the abnormal tests and Child-Pugh score ($p<0.0001$).[43] In their study, they found autonomic dysfunction in 69% of Child class B and C patients and 23% in class A patients ($p<0.0001$)

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This study also shows that bleeders have more incidence of autonomic dysfunction(61.7% parasympathetic & 14.7% sympathetic dysfunction) when compared to non bleeders (12.5 % parasympathetic & 6.2% sympathetic dysfunction). This has to be confirmed by further studies. Finally, considering the adverse prognostic implications of autonomic neuropathy reported in cirrhotics, further prospective studies involving a larger number of patients are warranted to delineate the factors responsible for the derangement and find remedial measures if possible.

CONCLUSION

This study has shown that autonomic dysfunction is very common in cirrhotic patients. The incidence of autonomic dysfunction also increases with increasing severity of liver disease. This study also highlights the importance of simple bedside investigations like ECG and clinical evaluation in early diagnosis of autonomic dysfunction.

The mortality of cirrhosis patients is partly related to poor autonomic responses to stressful events like sepsis or bleeding. On the basis of this evidence, it is suggested that consideration should be given for early liver transplantation in patients with autonomic neuropathy. These patients should also be given intensive care in the per-operative and post-operative period to decrease the mortality rate.

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PROFORMA

1. Name:

2. OP/IP Number:

3. Age:

4. Sex:

5. Diagnosis:

6. Etiology:

7. Duration:

8. Child’s grade:

9. H/O Postural giddiness:

10.H/O Smoking:

11.H/O Alcoholism:

12.H/O Bleed:

13.LFT:

14.Ascites:

15.Splenomegaly:

16.Pulse:

17.Blood pressure:

    1.supine:

    2.standing:

CARDIOVASCULAR SYSTEM

ELECTROCARDIOGRAM

1.Rate

2.R-R interval

3.P-R interval

4.QRS Duration

5.QRS Axis

6.QTc interval

7.E:I Ratio

8.Maximum- minimum heart rate

9.ST-T changes

ECHOCARDIOGRAPHY

MASTER CHART- STUDY GROUP

Sl.no	MGE.NO	Name	age	sex	h/o pos. giddiness	Etiology	Duration (years)	Child's	Rate bpm	RR	PR	QRS	axis	QTc	ST-T	E:I ratio	Pos.Hyp	bleed
1	1076/06	Arumugam	46	M	+	1	1	B	71	845	170	40	41	420	-	1.1	-	+
2	4001/05	Gomathy	35	F	+	4	1	B	94	638	100	60	90	400	-	1.06	-	+
3	994/06	Kavitha	28	F	-	4	1	B	94	638	160	60	25	455	-	1.09	-	+
4	894/06	Thaimani	55	F	-	2	1	B	101	594	132	80	32	456	-	1.11	-	-
5	5456/05	Elavarasi	16	F	-	2	1	B	103	582	140	60	45	408	+	1.13	-	+
6	5682/05	Rohini	13	F	-	4	2	A	97	619	135	100	18	457	+	1.12	-	+
7	61/06	Krisnan	16	M	-	3	1	B	119	504	108	40	23	501	-	1.07	-	+
8	6538/04	Panch	41	M	+	1	2	B	64	938	144	40	39	458	-	1.13	-	+
9	4538/05	Balakrisnan	57	M	-	4	3	B	66	909	120	60	-30	480	-	1.08	+	+
10	652/00	Velusamy	47	M	-	1	6	B	68	882	160	60	60	392	-	1.11	-	+
11	438/04	Natarajan	48	M	-	2	1	B	79	760	160	60	30	459	-	1.1	-	-
12	216/06	Munir	38	M	+	1	1	B	113	520	148	80	81	466	+	1.1	-	-
13	4136/05	Pitchai	36	M	-	1	2	B	82	732	144	40	65	434	-	1.09	-	+
14	406/06	Ravi	41	M	-	1	1	C	133	451	144	40	39	357	-	1.09	+	+
15	547/05	Sundaram	48	M	-	4	1	B	88	682	160	80	120	376	-	1.04	-	+
16	2349/04	Asokan	37	M	-	2	14	B	100	600	144	40	13	480	-	1.09	+	+
17	5799/03	Chandran	42	M	+	4	4	B	72	833	168	60	85	420	-	1.1	-	+
18	6329/05	Ramesh	45	M	-	1	2	B	63	952	132	40	76	432	-	1.1	-	-
19	106/06	Ravindran	29	M	-	1	4	B	67	896	136	40	5	448	-	1.11	-	+
20	286/06	Varadarajan	51	M	-	1	4	B	107	562	100	60	70	373	-	1.06	-	+
21	1168/05	Govindan	50	M	-	2	1	B	83	723	176	60	40	489	-	1.07	-	+
22	1034/05	Sures babu	32	M	-	1	1	C	110	545	140	40	20	476	-	1.07	-	+
23	1214/06	Kumar	40	M	-	1	1	A	88	682	140	60	30	439	-	1.14	-	+
24	2429/03	Mariammal	55	F	-	4	3	B	88	682	130	40	15	376	-	1.15	-	-
25	1082/06	Kasthuri	41	F	-	4	1	B	100	600	120	100	10	350	-	1.11	-	-

Sl.no	MGE.NO	Name	age	sex	h/o pos. giddiness	Etiology	Duration years	Child's	rate	RR	PR	QRS	axis	QTC	ST-T	E:I ratio	Pos.Hyp	bleed
26	3233/05	Naraiah	45	M	+	2	1	B	83	723	164	40	36	432	-	1.1	-	+
27	4568/04	Rajeswari	58	F	-	2	1	B	94	638	144	40	30	480	-	1.12	-	-
28	267/03	Parvathi	38	F	+	4	1	B	88	682	110	60	84	412	-	1.04	-	+
29	6284/05	Perumal	31	M	-	4	1	B	97	618	132	60	39	456	-	1.08	-	+
30	0009/04	Nazeer	14	M	-	3	1	B	115	521	110	60	30	480	-	1.08	-	-
31	4008/05	Palani	55	M	-	4	3	B	75	800	120	60	-36	438	-	1.09	+	-
32	3367/05	Abu becr	40	M	+	1	1	B	107	562	148	60	76	460	+	1.1	-	-
33	4847/05	Satish	14	M	-	2	1	B	100	600	144	45	40	410	+	1.14	-	-
34	4441/04	Balaji	13	M	-	4	2	A	94	638	135	60	20	450	+	1.13	-	-
35	3853/03	Gunalan	37	M	-	1	4	B	68	882	136	60	8	450	-	1.12	-	-
36	5252/05	Guru nadan	42	M	+	1	2	B	66	909	144	60	40	460	-	1.12	-	-
37	2832/04	Hari babu	35	M	-	1	2	B	80	750	144	40	66	436	-	1.09	-	+
38	45598	Jayadev	40	M	-	1	2	B	84	714	140	60	60	430	-	1.08	-	+
39	1034/02	Jayalaxmi	40	F	-	4	1	B	102	588	124	60	12	352	-	1.11	-	-
40	3980/05	Kalifath	33	M	-	1	1	C	108	555	144	40	18	474	-	1.06	-	+
41	2404/01	Katija	56	F	-	4	3	B	90	667	128	60	18	372	-	1.13	-	+
42	2759/05	Balamurugan	41	M	-	1	1	A	86	698	136	40	32	442	-	1.12	-	+
43	5394/03	Durairaj	49	M	-	4	1	B	91	659	154	60	116	372	-	1.06	-	+
44	64703	Doss	42	M	-	1	1	C	120	500	136	80	42	350	-	1.08	+	+
45	650/06	Ellappan	49	M	-	1	4	B	110	545	96	60	66	372	-	1.07	-	+
46	61472	Jayavel	38	M	-	2	9	B	98	612	140	40	17	456	-	1.07	+	+
47	4851/04	Sampath	45	M	-	1	4	B	70	857	156	60	56	390	-	1.12	-	+
48	3115/05	Anthoni	45	M	+	1	1	B	74	811	168	40	72	416	-	1.12	-	+
49	4439/05	Babu	50	M	-	2	1	B	85	706	174	40	42	485	-	1.09	-	+
50	3125/03	Balaji 1	44	M	-	1	2	B	65	923	130	80	80	430	-	1.12	-	-

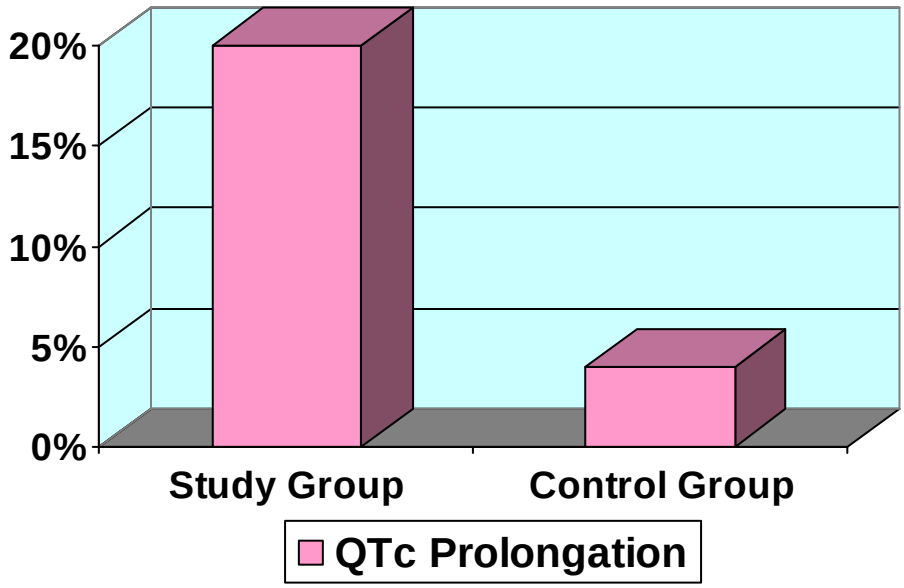
Etiology:1- alcoholism, 2- viral, 3- metabolic, 4- others

MASTER CHART- CONTROL GROUP

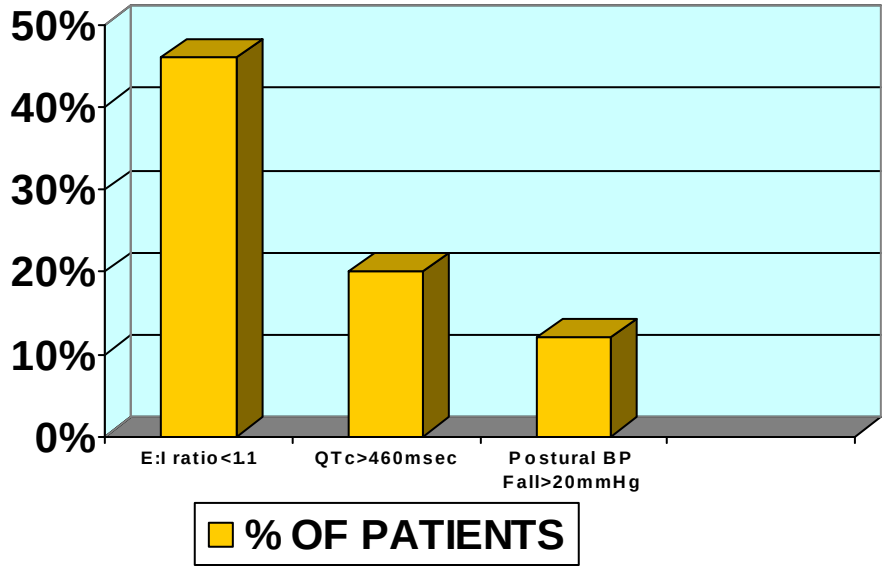
Sl.no	Name	IP no	Age	Sex	H/o post. giddiness	Pulse	Post hypo	Rate	RR	PR	QRS	QRS axis	QTc	ST-T
1	Manalan	245364	47	M	-	76	-	76	790	124	60	88	352	+
2	Jaya	256021	37	F	-	66	-	66	914	164	60	72	370	-
3	Ravi	100236	46	M	-	76	-	76	790	184	60	64	312	-
4	Palani	105638	45	M	-	83	-	83	723	160	60	46	330	-
5	Ram kumar	100114	37	M	-	58	-	58	1035	138	80	60	396	-
6	Santhanam	225472	36	M	-	78	-	78	769	140	60	64	364	-
7	Muthiah	105488	41	M	-	100	-	100	600	120	70	90	372	-
8	Udayan	16734	48	M	-	92	-	92	652	118	40	72	363	+
9	Mary	201965	53	F	-	62	-	62	968	146	60	43	405	+
10	Balakumar	10087	42	M	-	71	-	71	845	142	60	47	409	-
11	Banumathi	29475	38	F	-	68	-	68	882	120	60	61	371	-
12	Ilavarasu	25678	48	M	-	66	-	66	909	158	40	53	375	-
13	Barathi	217131	45	M	-	72	-	72	833	140	60	28	374	-
14	Sathya	29587	28	F	-	80	-	80	750	142	40	3	364	-
15	Sivagami	29544	57	F	-	86	-	86	698	124	40	28	330	-
16	Selvam	27563	44	M	-	68	-	68	882	156	60	52	388	-
17	Sivaraj	16574	43	M	-	78	-	78	769	120	60	24	360	-
18	Appusamy	28536	48	M	-	70	-	70	857	130	40	0	398	-
19	Madavan	25567	40	M	-	76	-	76	790	148	60	30	345	-
20	Balan	25638	46	M	-	80	-	80	750	123	60	44	331	-
21	Santhy	182309	42	F	-	90	-	90	667	120	60	26	372	-
22	Kamal	19986	44	M	-	60	-	60	1000	124	60	36	336	+
23	Muniammal	24378	58	F	+	82	-	82	732	124	60	12	453	-
24	Nagaraj	34562	52	M	-	72	-	72	833	140	60	70	366	+
25	Palraj	102456	38	M	-	72	-	72	833	128	80	62	346	-

Sl.no	Name	IP no	Age	Sex	H/o post. giddiness	Pulse	Post hypo	Rate	RR	PR	QRS	QRS axis	QTc	ST-T
26	Begam	28891	56	F	+	80	-	80	750	128	70	24	336	-
27	Sanmugam	199827	35	M	-	72	-	72	833	124	84	40	384	-
28	Eswar	42336	42	M	-	68	-	68	882	142	46	54	380	-
29	Muthammal	102455	41	F	-	82	-	82	732	164	60	32	360	-
30	Gandhi	178203	43	M	-	92	-	92	652	160	70	64	372	-
31	Pandi	132456	40	M	-	80	-	80	750	134	64	2	378	-
32	Anthoni	27420	48	M	-	90	-	90	667	144	72	60	406	+
33	Janakiraman	133245	46	M	-	56	-	56	1071	164	46	90	416	-
34	Ramesh	132457	29	M	-	58	-	58	1034	154	60	76	320	-
35	Riwan	35679	49	M	-	86	-	86	698	148	80	100	396	-
36	Periyasamy	23158	36	M	-	72	-	72	833	146	48	43	352	-
37	Kuppan	67890	48	M	-	87	-	87	670	148	54	28	372	-
38	Munusamy	56429	41	M	-	89	-	89	674	129	64	47	346	-
39	Baskar	83256	36	M	-	76	-	76	790	164	70	30	360	+
40	Vedachalam	72891	55	M	-	70	-	70	857	140	64	45	385	-
41	Murali	15347	40	M	-	86	-	86	698	126	42	50	405	-
42	Gangadar	23145	32	M	-	62	-	62	968	184	72	70	372	-
43	Farida	12684	17	F	-	108	-	108	560	200	78	60	474	-
44	Rahman	35242	29	M	-	58	-	58	1034	136	88	46	391	-
45	Priya	24567	18	F	-	77	-	77	779	148	70	70	498	-
46	Kannan	14425	55	M	-	72	-	72	833	140	64	39	382	-
47	Sekar	12987	14	M	-	88	-	88	682	153	74	24	348	-
48	Devaraj	53426	16	M	-	78	-	78	769	168	104	74	443	-
49	Arun	23145	15	M	-	86	-	86	698	147	82	72	396	-
50	Krishnan	9437	15	M	-	84	-	84	714	164	60	31	364	-

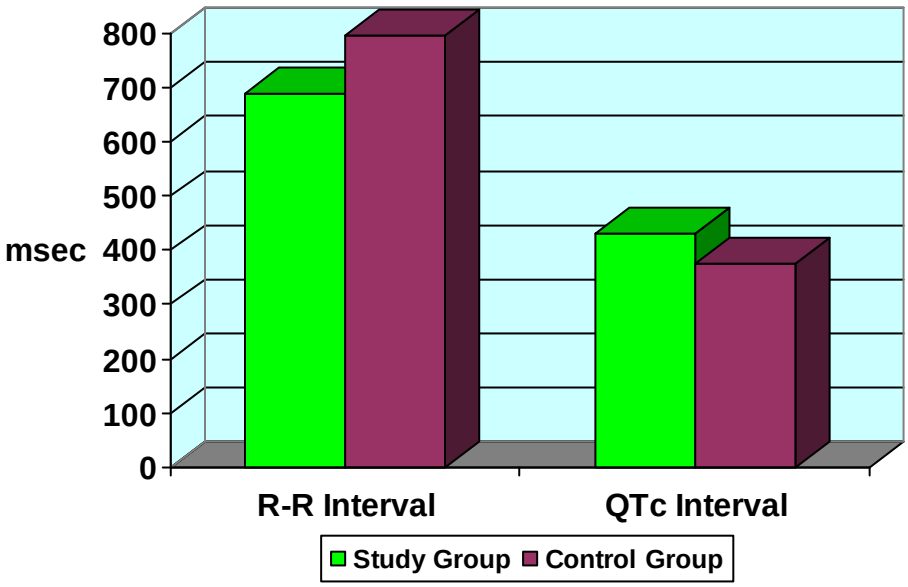
INCIDENCE OF QTc PROLONGATION



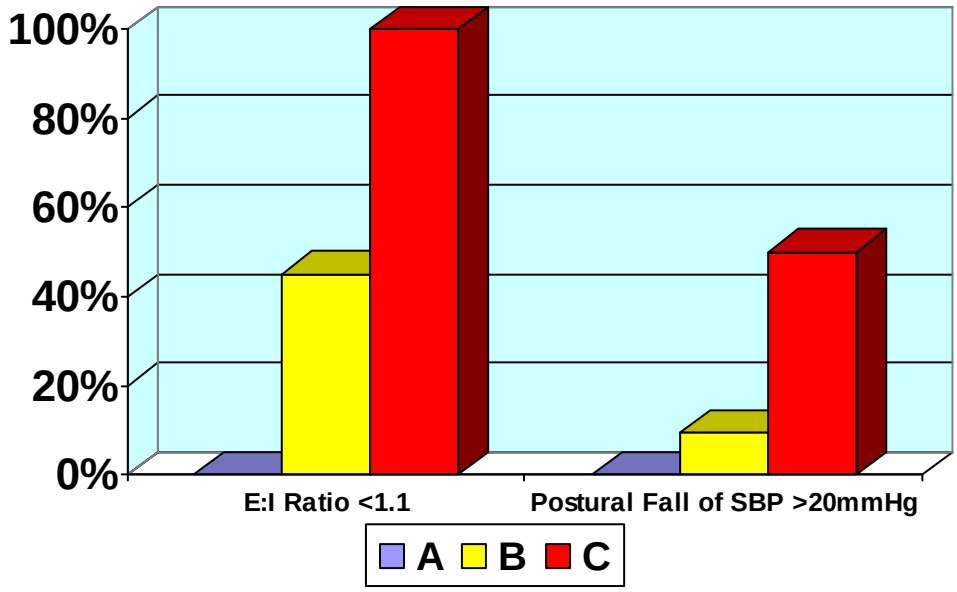
DYSAUTONOMIA IN CIRRHOTICS



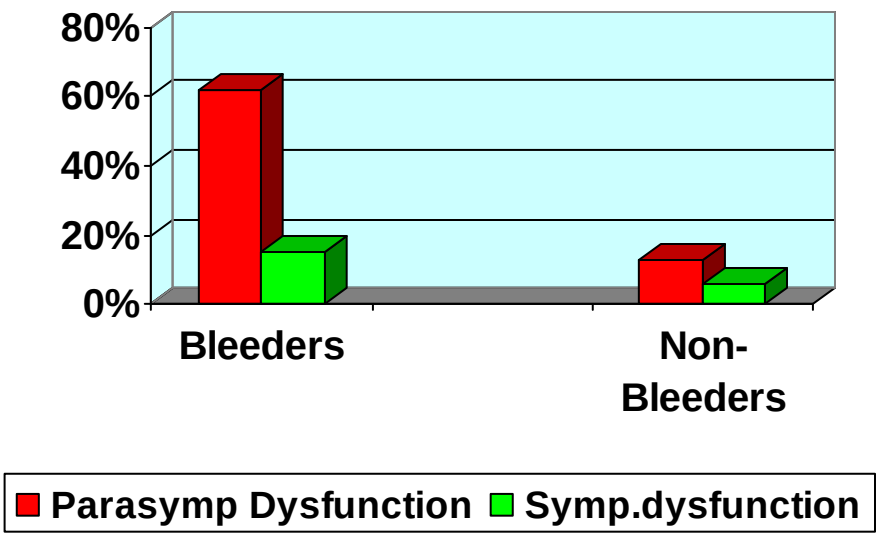
COMPARISON OF ECG PARAMETERS



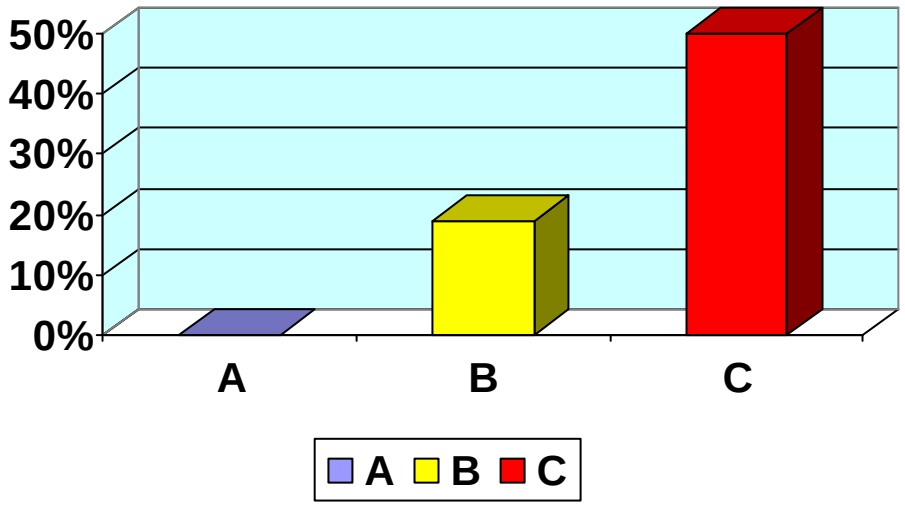
DYSAUTONOMIA VS CHILD'S GRADING



DYSAUTONOMIA Vs GI BLEED



QTc PROLONGATION Vs CHILD'S GRADING



QTc INTERVAL PROLONGATION